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Filed : February 19, 1999

Please add the following new claim:

24. (NEW) A high throughput chemical screener comprising:  
a chemical library comprising storage locations for at least approximately 1000 multi-well plates, and at least approximately 100,000 addressable chemical storage locations each containing a different chemical;  
a computer controlled chemical well retriever for programmable selection and retrieval of selected ones of said chemical wells;  
a parallel transport path coupled to said chemical library; and  
a plurality of asynchronously operable automated liquid handling devices coupled to said transport path.

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#### REMARKS

Applicants have amended claims 1, 8, and 20, and have cancelled claims 4, 5, 7, 9 and 13-19, without prejudice. Applicants respond below to rejections and objections raised by the Examiner in the Office Action of August 29, 2000.

#### I. Information Disclosure Statement

The Examiner indicates that certain documents, which are of record in the parent application Serial No. 08/858,016 and which are listed on the Information Disclosure Statement of May 24, 1999, are missing. Applicants regret the inconvenience to the Examiner and have attached herewith a copy of the missing documents.

#### II. Rejections under 35 U.S.C. § 112

Claims 8-12 stand rejected under 35 U.S.C. § 112 for allegedly being indefinite. The Examiner alleges that the limitation "programmably integrated" is unclear.

Applicants respectfully traverse. The specification at page 8, lines 23-27, states that the present invention includes ensembles of integrated components to form a system. Thus, the word "integrated" is taken to mean an ensemble of components linked together to form a system. The phrase "programmably integrated" would then mean that such act of integration is carried

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out through a computer program. Thus, if two components are "programmably integrated," then the operation of those two components in the system is linked through a computer program.

Applicants respectfully maintain that this definition is clear and unambiguous to those of skill in the art and respectfully request that the rejection be withdrawn.

### **III. Rejections under 35 U.S.C. § 102**

Claims 8, 10-12, and 17-19 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ishibashi (USP 5,087,423). Claims 8, 10, and 22 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by each of Ashihara et al. (USP 5,158,895) and MacIndoe (USP 5,332,549). Claims 8, 10-12, and 17-19 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Mimura (USP 5,902,549).

In view of the above amendments, the Examiner's rejection of Claims 17-19 is now moot.

Without acquiescing to the Examiner's characterization of the references with respect to Claim 8, Applicants have amended Claim 8 by incorporating the limitations of Claim 9. Claims 10-12 depend directly or indirectly from claim 8 and incorporate all of its limitations.

The Examiner has not pointed to any reference which anticipates or renders obvious the limitations of amended Claim 8, in particular the rate of sample screening of at least 50,000 per day. Applicants respectfully maintain that no *prima facie* case of anticipation or obviousness has been made out.

With respect to the rejection of Claim 22, Applicants respectfully traverse. The last two lines of the claim describe the element of "a chemical storage buffer on the chemical retriever." Such a chemical well retriever is illustrated in Figure 14 of the application and is described in the specification at page 74, line 29 through page 75, line 8. None of the cited references describe or teach a storage buffer on the retriever as claimed. The buffer on the retriever reduces sample retrieval time by allowing the retriever to pull multiple plates from one section of the storage module prior to travelling back to the transport module. The applicant respectfully submits that Claim 22 is therefore in condition for allowance.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

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**IV. Rejections under 35 U.S.C. § 103**

Claims 1-7, 13-16, and 20-23 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Ishibashi in view of MacIndoe.

In view of the above amendments, the Examiner's rejection of Claims 13-16 is now moot.

With respect to the rejections of Claims 1-7 and 20-23, Applicants respectfully traverse. In the rejection of these claims, the Examiner contends that MacIndoe, Jr. teaches the automated well retrieval from a chemical library that is missing from Ishibashi. However, the "library" the Examiner is referring to in MacIndoe, Jr. is an assay module library, not a chemical sample library. This is made clear by the text of MacIndoe, Jr. at column 5, line 57 through column 6, line 11. As described in this portion of the MacIndoe Jr. reference, samples to be tested are manually loaded in the system of MacIndoe Jr., and are processed in the order in which they are loaded by the operator. *manually*

In contrast, independent Claim 20 recites a chemical library in combination with "a computer controlled chemical well retriever for programmable selection and retrieval of selected ones of said chemical wells." This is not shown or described in Ishibashi, MacIndoe Jr., or any other reference currently of record. In the references specifically cited, for example, sample chemicals are processed serially in the order they are placed on the device by the operator. Programmable retrieval of selected chemicals is not taught or suggested. In the above referenced portion of MacIndoe, a sample loading process is described wherein trays of samples are loaded by the operator in a given order, and they are processed serially in that order. The disclosure of Ishibashi is similar. In Ishibashi, "samples No. 1 No. 3 are contained in sample cups and arranged in the sampler 4 in this order" (column 4, lines 36-37).

Furthermore, Claim 20 recites that the chemical library comprises storage locations for at least 1000 multi-well plates. In the Office Action, the Examiner characterizes this limitation as an obvious matter of design choice defining merely a "change in size" relative to the prior art. Applicants note that it has been held that a mere change in size will not confer patentability when that is the only claimed feature distinguishing the invention from the prior art. M.P.E.P. 2144.04(d). In Claim 20, however, the limitation relating to the size of the library is coupled with limitations on the system that for the first time allow for the processing of such large chemical libraries in a reasonable amount of time. Thus, prior to applicant's invention of the *no obvious*

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combination of features recited in Claim 20, one of ordinary skill in the art would not be motivated to produce or use a chemical library of the size recited in Claim 20, nor would it have been considered desirable. Thus, more than a mere change in size is being claimed, and the applicants respectfully submit that the combination of elements of Claim 20, including the recitation of library size, defines patentable subject matter.

In addition, the 1000 multi-well plates of Claim 20 store at least approximately 1000 different chemical compounds. None of the cited references, either individually or in combination, teach or suggest having a storage location for a myriad of different compounds.

Turning now to independent Claim 1, this claim is directed to a system including a library having storage locations for approximately 3,000 multi-well plates and screening approximately 25,000 chemical samples in a 24 hour period. As with Claim 20 discussed above, more than a mere change in size is being claimed. Claim 1 as amended includes a computer controlled chemical well retriever, an automated, bi-directional, and parallel transport path, a stacking storage buffer, and a plurality of asynchronously operable automated liquid handling devices. As described above with reference to Claim 20, the cited prior art does not teach or suggest the combination of these elements. Each of these elements contributes to the capacity of the system to process large numbers of samples in a short amount of time, and that for the first time, make a chemical library of the size claimed useful in a compound screening system. Allowance of amended Claim 1 is thus respectfully requested.

Independent Claim 22 has been discussed above with reference to anticipation by Ashihara and MacIndoe, Jr. It is submitted that Ishibashi does not cure the deficiencies of these references as discussed above, and reconsideration and withdrawal of the rejection is respectfully requested.

Claims 2-7, 21, and 23 depend from independent Claims 1, 20, and 22 respectively, and it is submitted that these claims are patentable for at least the same reasons as discussed above for their independent base claim.

#### **V. Double Patenting**

Claims 1-23 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-30 of Stylli et al., USP 5,985,214. Applicants have filed a terminal disclaimer herewith, disclaiming the term of any patent issued

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from the present application extending beyond the term of the 5,985,214 patent. The terminal disclaimer obviates the rejection.

### CONCLUSION

The applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims for patentability purposes pursuant to statutory sections 102, 103 and/or 112, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested.

Any claim amendments which are not specifically discussed in the above remarks are not made for patentability purposes, and it is believed that the claims would satisfy the statutory requirements for patentability without the entry of such amendments. These amendments have only been made to increase claim readability, to improve grammar, and to reduce the time and effort required of those in the art to clearly understand the scope of the claim language.

If the Examiner has any questions which may be answered by telephone, he is invited to call the undersigned directly.

Respectfully submitted,

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Dated: January 29, 2001

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